Exercises - PASB 2020

Hands-on session on FBA and TFA analysis of a genome-scale metabolic models as well as modeling kinetics using ordinary differential equations.

Modeling flux distributions in metabolic networks

For this exercise use the model file **E.coli GEM and Yeast.mat** you find on moodle.

Part 1: Load the models for *E. coli* and the yeast *Saccharomyces cerevisiae*. Compare the number of metabolites, reactions, and genes in the two models. Do you see any other difference between these models?

Part 2: Simulating Growth. Compare the growth rate of *E. coli* growing on 10 mmol/gDW/hr glucose in aerobic and anaerobic conditions. What are the differences? Do the same analysis for the yeast.

Part 3: Investigate trade-off between nutrient uptake and growth rate in *E. coli*. Calculate therefore, the growth for oxygen and glucose uptake rates between 0 and 10 mmol/gDW/hr. Plot the resulting surface in a 3D surface plot. Describe and discuss the results: How are the slopes behaving along the two axes? How can you interpret these results?

Part 4: Investigate the phenotypes across the different oxygenation and glucose uptakes. Use the data points generated for Part 2 and for each, constrain the growth to be at it maximum. Vary all boundary reactions (i.e. met -> …) and find which are the metabolites that **have to be** secreted.

Part 5: Solve part 1-3 one time using TFA (only for *E. coli*). FBA will be less computationally expensive as it will contain less constraints. How the results are different?

Part 6: The metabolomics data file, “ecoli_metabolomics_data.csv”, contains measured metabolite concentrations in [M] from Park et al.[1]. Uses these metabolite concentrations to constraint the cytosolic log-concentrations within the TFA model. Simulate growth and investigate the trade-off between oxygen, glucose uptake and growths. Do you find differences?

[1] Park JO, Rubin SA, Xu YF, et al. Metabolite concentrations, fluxes and free energies imply efficient enzyme usage. *Nat Chem Biol*. 2016;12(7):482-489. doi:10.1038/nchembio.2077